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NCIC H P V
. Sent by: Mary-Beth Weaver

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To: NCIC HPV, moran.matthew@epa.gov
cc:
cc:
Subject: Environmental Defense comments on 2-Butene-1,4-diol (CAS# 110-64-5)

Richard_Denison@environmentaldefense.org on 06/02/2003 02:05:22 PM

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Subject: Environmental Defense comments on 2-Butene-1,4-diol (CAS# 110-64-5)

(Submitted via Internet 6/2/03to oppt.ncic@epa.gov, hpv.chemrtk@epa.gov, boswell.karen@epa.gov, chem.rtk@epa.gov, lucierg@msn.com and erauckman@charter.net)

Environmental Defense appreciates this opportunity to submit comments on the robust summary/test plan for 2-Butene-1,4-diol (CAS# 110-64-5).

The test plan and robust summaries were submitted by the 2-butene-1,4-diol (2-BD) consortium and were prepared by the Toxicology and Regulatory Affairs Group. This submission, like the others from this group, is accurate, complete, informative and well-written. 2-BD, according to the sponsor, is used as an intermediate in the synthesis of numerous products. Those products are not identified in the test plan although they are referenced. We recommend that the referenced applications be described in the test plan for the purpose of improving public access to such information. The sponsor states that there are no known uses of 2-BD in consumer products.

The test plan proposes that a combined repeat dose/reproductive/developmental toxicity study be conducted on 2-BD because there are no existing studies of appropriate quality on these endpoints. We agree with this proposal. We also recommend that a fish toxicity study also be conducted due to the poor quality of the existing studies presented in the robust summaries. Specific comments are as follows:

1. 2-BD is water soluble and readily biodegraded, and it should not accumulate in the environment. Existing data on physiochemical properties and environmental fate and distribution are adequate to fulfill HPV requirements.

2. Fish toxicity studies presented in the robust summaries are difficult to evaluate. The summary of one study provides very limited experimental detail, while the other has several deficiencies that are identified in the robust summary. These deficiencies preclude use of this study to meet the fish toxicity endpoint. Unless sufficient details can be provided on the first study, which like the second was not conducted under GLP, then we recommend that the sponsor conduct an additional fish toxicity study.

3. Existing data on acute toxicity in animals and genetic toxicity are adequate to fulfill HPV requirements. These studies indicate that 2-BD has moderate toxicity but apparently possesses little or no genotoxicity.

4. The sponsor presents considerable information on metabolic activation/deactivation pathways for 2-BD. This information is useful as it helps in understanding dose-response relationships and target organ

toxicity. These data also reveal that maleic acid is a major metabolite of 2-BD.

5. There are no existing repeat dose studies of appropriate quality. In one of the studies all the rats died prior to completion of the experiment. There are also no existing reproductive or developmental toxicity studies, so the sponsor has proposed that a combined repeat dose/reproductive/developmental toxicity study be conducted. We agree with this proposal and we also agree with the sponsor that the proposed study, along with existing studies on maleic acid, should be adequate to fulfill requirements for these three endpoints.

Thank you for this opportunity to comment.

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